

REMARKS

Claims 1, 2, 5-7, 19-23, 26-29, 32-36, 38, 39 and 44-51 are pending in the present Application. Claims 4, 8-17, 20, 25, 31, 34, 37 and 40-43 have been cancelled, Claims 1, 5-7, 21, 22, 35 and 36 have been amended, and Claims 52-59 have been added, leaving Claims 1, 2, 5-7, 19, 21-23, 26-29, 32, 33, 35, 36, 38, 39, and 44-59 for consideration upon entry of the present Amendment.

Support for the amendment to claims 1, 22, 29 and 36 can be found in paragraph [0067].

Claims 5-7, 21 and 35 have been amended merely to change their dependency.

Support for new claims 52-54 can be found in paragraph [0066].

Support for new claims 55-59 can be found in paragraph [0067].

Reconsideration and allowance of the claims are respectfully requested in view of the above amendments and the following remarks.

Information Disclosure Statement

Applicants again note that the Examiner has not considered the art submitted in the Information Disclosure Statements filed:

November 6, 2003, November 14, 2003, February 9, 2004, April 12, 2004,
September 30, 2004, and December 19, 2005.

Applicants respectfully request that the art submitted in these Information Disclosure Statements be considered and a fully initialed PTO Form A820 be returned to the Applicants.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 5-7 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the claims are incomplete since they depend from a deleted claim.

Claims 5-7 have been amended to depend from claim 1.

Reconsideration and withdrawal of this rejection are respectfully requested.

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 1-2, 5-7, 19, 20-23, 26-29, 32, 34-36, 38 and 39 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Japanese Publication No. JP-09-176011 in view of U.S. Patent No. 6,498,188 to Camden. Applicants respectfully traverse this rejection.

According to the Examiner, JP 09-176011 discloses the use of various flavonoids such as wogonin to treat cancer. In paragraph [0039], for example, this reference does appear to teach the use of wogonin to treat gastric, colon, renal, and prostate cancer cell lines, but does not teach treatment of cancer in a human patient. The flavonoids, including wogonin, however, are not used to treat cancer per se, but instead are used to control the expression of the heat shock protein HSP 27 so that the biosynthesis of that protein is decreased. This allows for more effective thermotherapy, that is, once the heat shock protein level has been reduced, the cancer cells are more susceptible to apoptosis induced by warming. Thus, wogonin is not used to treat cancer, but instead is used to “reinforce the effectiveness of chemotherapy.” (paragraph [0041]) It is disclosed in paragraph [0030] to use 0.1-80 wt% of the flavonoid as a synthetic inhibitor. JP 09-176011 does not teach the combination of flavonoids with non-phytoestrogen anti-cancer agents or immunomodulators.

The Examiner combines JP 09-176011 with Camden which teaches carbamate and thiocarbamate compounds used against tumors which have been removed from the human and grown in cell culture. There are no combination therapies shown and, rather than demonstrating that combination therapies work with the disclosed carbamates and thiocarbamates, Camden simply demonstrates that the carbamates and thiocarbamates disclosed can kill cells. Camden does appear to teach the use of immunomodulators to increase the efficacy of the thiocarbamates. (Col. 11, ll. 33-37)

For an obviousness rejection to be proper, the Examiner must meet the burden of establishing that all elements of the invention are disclosed in the prior art; that the prior art relied upon, or knowledge generally available in the art at the time of the invention, must provide some suggestion or incentive that would have motivated the skilled artisan to modify a reference or combined references. *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). “A patent composed

of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR Int’l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 (2007). To find obviousness, the Examiner must “identify a reason that would have prompted a person of ordinary skill in the art in the relevant field to combine the elements in the way the claimed new invention does.” *Id.*

In order to arrive at the claimed compositions, the Examiner combines JP 09-176011, which teaches the use of phytoestrogens in vitro in cancer cells, with Camden which teaches combination chemotherapies with carbamate and thiocarbamate compounds, and not phytoestrogens. In making the rejection, the Examiner alleges that combination chemotherapies are well-known and relies on Camden for this teaching. The teaching of Camden, however, is limited to the teaching that carbamate and thiocarbamate compounds can be combined with additional chemotherapeutic agents. Camden, as admitted by the Examiner, specifically fails to teach the particular advantage of combining a phytoestrogen with an anti-cancer agent and/or an immune stimulant. There is no teaching in the cited references of any advantage of combining phytoestrogens with additional chemotherapeutic agents. Thus, one important difference between the present claims and the cited references is that the cited references do not suggest any advantage of combining phytoestrogens with an additional chemotherapeutic agent to treat cancer.

In an effort to advance prosecution, the independent claims have been amended to specify a composition consisting essentially of a phytoestrogen, at least one second anti-cancer agent and an immune stimulant. The inventor of the present application has found that the combination of three active agents, a phytoestrogen such as wogonin, at least one second anti-cancer agent and a immune stimulant, has unexpectedly beneficial properties. The use of “consisting essentially of” in this claim allows for the addition of inert ingredients such as pharmaceutical excipients to the composition, but limits the active ingredients to phytoestrogens, one or more additional anti-cancer agents and an immune stimulant. The synergy between a phytoestrogen such as wogonin, a second anti-cancer agent such as oridonin and an immune stimulant such as beta-pachyman provides especially beneficial results in the treatment of hormone-related cancers such as prostate cancer, breast cancer, endometrial cancer, colon cancer, lung cancer, bladder cancer, testicular cancer, ovarian cancer, thyroid cancer, or bone cancer. In addition, the inventor of the present

application has found that it is particularly advantageous to use higher concentrations of phytoestrogen such as wogonin in the synergistic three-part compositions than had previously been reported.

The Examiner is also directed to new claims 52-59 which specify the additional anti-cancer agents and immune stimulants in the composition. JP 09-176011 and Camden do not render these particular combinations of active agents obvious.

Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 1-2, 5-6, 19, 20, 22, 23, 26, 29, 32, 34, 36, and 38 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over JP 09-176011 in view of U.S. Patent No. 6,413,535 to Steiner et al (hereinafter “Steiner et al ‘535”). Applicants respectfully traverse this rejection.

Steiner is directed to chemoprevention of prostate cancer using phytoestrogens and other anti-cancer agents. (Col. 5, ll. 11-30) Steiner does not teach the use of wogonin. Steiner also appears to teach the use of adjuvants to enhance the immune response to an antigen. (Col. 7, ll. 63-64.

In making the rejection, the Examiner states: “It would have been obvious to one of ordinary skill in the art to combine the ingredients . . . of the secondary reference to the composition of the primary reference since motivation would stem from the reasonable expectation of treating cancer with a combination of drugs already known to be useful for the treatment of cancer.” (October 14, 2008 Office Action, p. 5)

In an effort to advance prosecution, the independent claims have been amended to specify a composition consisting essentially of a phytoestrogen, at least one second anti-cancer agent and an immune stimulant. The inventor of the present application has found that the combination of a phytoestrogen such as wogonin, at least one second anti-cancer agent and a immune stimulant has unexpectedly beneficial properties. The use of “consisting essentially of” in this claim allows for the addition of inert ingredients such as pharmaceutical excipients to the composition, but limits the active ingredients to phytoestrogens, one or more additional anti-cancer agents and an immune stimulant. The synergy between a phytoestrogen such as wogonin, a second anti-cancer agent such as oridonin and an immune stimulant such as beta-pachyman provides especially beneficial results in the treatment of hormone-related cancers such as prostate cancer, breast

cancer, endometrial cancer, colon cancer, lung cancer, bladder cancer, testicular cancer, ovarian cancer, thyroid cancer, or bone cancer.

The Examiner is also directed to new claims 52-59 which specify the additional anti-cancer agents and immune stimulants in the composition. JP 09-176011 and Steiner do not render this particular combination of active agents obvious.

Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 21, 27, 35, 39, 50 and 51 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over JP 09-176011 and Steiner, in view of Japanese Application No. 11-244597.

JP 11-244597 is relied on for the teaching of an extract of *Ganoderma lucidum* as a component in an anti-cancer composition.

JP 11-244597 does not, however, cure the defects of JP 09-176011 and Steiner. As explained above, the present claims have been amended to specify a composition consisting essentially of a phytoestrogen such as wogonin, at least one second anti-cancer agent and a immune stimulant. Such a composition containing the claimed amount of phytoestrogen has unexpectedly beneficial properties in the treatment of cancers, particularly hormone-related cancers. The combination of JP 09-176011, Steiner and JP 11-244 does not render obvious the claimed composition.

The Examiner is also directed to new claims 52-59 which specify the additional anti-cancer agents and immune stimulants in the composition. JP 09-176011, Steiner and JP 11-244 do not render this particular combination of active agents obvious.

Reconsideration and withdrawal of this rejection are requested.

Claims 1-2, 5-7, 19, 20-23, 26, 27-29, 32-36, 38, 39, and 46-51 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over U.S. Patent No. 5,665,393 to Chen et al. Applicants respectfully traverse this rejection.

The Examiner has provided no explanation of the substance of this rejection.

Chen et al. is directed to the discovery of an eight-part composition for treating prostate cancer comprising:

Panax pseudo-ginseng Wall (gensenoside, anti-cancer agent)

Isatis Indigotica Fort (immune stimulant)

Ganoderma lucidum Karst (source of anti-cancer agent; immune stimulant)

Dendranthema morifolium Tzvel (anti-viral agent)

Glycyrrhiza glabra L. (source of isoliquiritigenin)

Scutellaria baicalensis Georgi (source of baicalin, anti-cancer agent; source of wogonin, phytoestrogen)

Rabdosia robescens and (source of oridonin, anti-cancer agent)

Serenoa repens. (anti-prostate hyperplasia activity)

Thus, the composition of Chen et al. contains components that the present composition does not have, specifically an anti-viral agent and an anti-prostate hyperplasia agent. By amending the claims of the present application to “consisting essentially of” the present claims eliminate these additional active agents. There is no teaching or suggestion in Chen et al. that increasing the concentration of phytoestrogen and eliminating two components from the eight-part composition would provide a composition with improved anti-cancer activity. Dr. Chen, inventor of the preset application as well as U.S. Patent No. 5,665,393, unexpectedly found that a three-part composition containing a relatively high amount of phytoestrogen such as wogonin as presently claimed had superior anti-cancer activity to the 8-part composition disclosed in U.S. Patent No. 5,665,393.

It is also of note that because of the extraction techniques used in Chen et al., the amounts of phytoestrogen (either wogonin or isoliquiritigenin) are much lower than the presently claimed amounts. As can be see in the Examples of the present application, the composition of Chen et al. was used as a source of purified wogonin. Figure 3 shows a mass spectrum of purified wogonin. Although the composition of Chen et al. is suitable for its intended purpose, Dr. Chen found that by purifying a phytoestrogen such as wogonin and using it at relatively high concentrations along with an anti-cancer agent and a immune stimulant, that a composition with improved anti-cancer activity compared to that in Chen et al. was produced.

For at least the foregoing reasons, reconsideration ad withdrawal of this rejection are requested.

Claims 1-2, 5-7, 19, 20-23, 26, 27-29, 32-36, 38, 39, and 46-51 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over International Publication No. WO 98/09615. Applicants respectfully traverse this rejection.

Wang is the PCT publication corresponding to Chen et al. As the disclosures of these two references are identical, the arguments applied above to Chen et al. also apply here

For at least the foregoing reasons, reconsideration and withdrawal of this rejection are requested.

Claims 44 and 45 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over U.S. Publication No. 2002/0182274 to Lu. Applicants respectfully traverse this rejection.

Lu is directed to the treatment of cancer using compositions containing fermented soy extracts (Abstract). It is not clear what the actual composition of the fermented soy extract of Lu is, however, Lu appears to suggest that the extract has immune promoting functions [0038-0039] and anti-cancer functions [0043-0047].

Because claims 44 and 45 are dependent claims, this rejection is not understood. Applicant is assuming that because Lu does not teach the use of wogonin, that the Examiner has meant to combine Lu with a reference that teaches wogonin.

Even if Lu contained all elements of the claimed composition, the relationship of Lu to the claim element of taxol-resistant cancers is not understood. While Lu does appear to disclose the treatment of ovarian cancer, Lu does not disclose the treatment of taxol-resistant ovarian cancer. The examiner alleges that any method to treat ovarian cancer is a method to treat taxol-resistant ovarian cancer. This is an oversimplification of the problem of treating taxol-resistant cancers. As is known in the art, once a cancer is resistant to one agent, it is often resistant to multiple agents. Thus, treating taxol-resistant cancer is much more challenging than treating non-resistant cancer. The identification of a composition suitable for the treatment of taxol-resistant cancer is a substantial contribution.

If this rejection is to be maintained in the next office action, the Examiner is respectfully requested to completely explain the rejection.

Reconsideration and withdrawal of this rejection are respectfully requested.

Obviousness Double Patenting

Claims 1-2, 5-7, 19, 20-23, 26, 27-29, 32-36, 38, 39, and 46-51 have been rejected under the judicially created doctrine of obviousness-type double patenting over Claims 7-9 of U.S. 5,665,393 to Chen et al.

Claims 7-9 of Chen et al. require an 8-part composition including an anti-viral gent and a anti-prostate hyperplasia agent. By amending the claims of the present application to “consisting essentially of” the present claims eliminate these additional active agents. Thus the present claims are patentably distinct from the claims of Chen et al.

Reconsideration and withdrawal of this rejection are respectfully requested.

It is believed that the foregoing amendments and remarks fully comply with the Office Action and that the claims herein should now be allowable to Applicants. Accordingly, reconsideration and withdrawal of the objection(s) and rejection(s) and allowance of the case are respectfully requested.

If there are any additional charges with respect to this Amendment or otherwise, please charge them to Deposit Account No. 06-1130.

Respectfully submitted,

CANTOR COLBURN LLP

/Karen A. LeCuyer/

By _____

Karen A. LeCuyer

Registration No. 51,928

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CANTOR COLBURN LLP
20 Church Street, 22nd Floor
Hartford, CT 06103
Telephone (860) 286-2929
Facsimile (860) 286-0115
Customer No.: 23413